# NATIONAL GUIDELINE CLEARINGHOUSE™ (NGC) GUIDELINE SYNTHESIS

## SCREENING FOR LUNG CANCER

### Guidelines

1. **American Cancer Society (ACS)**. Update 2001--Testing for early lung cancer detection. In: American Cancer Society guidelines for the early detection of cancer. CA Cancer J Clin 2001 Jan-Feb;51(1):38-75. [181 references]
2. **American College of Chest Physicians (ACCP)**. Screening for lung cancer: ACCP evidence-based clinical practice guidelines. Chest 2007 Sep;132(3 Suppl):69S-77S. [41 references]
3. **Canadian Task Force on Preventive Health Care (CTFPHC)**. Screening for lung cancer: updated recommendations from the Canadian Task Force on Preventive Health Care. London (ON): Canadian Task Force on Preventive Health Care (CTFPHC); 2003 Aug. 22 p. [28 references]
4. **U.S. Preventive Services Task Force (USPSTF)**. Lung cancer screening: recommendation statement. Ann Intern Med 2004 May 4;140(9):738-9. [2 references]

### INTRODUCTION

A direct comparison of American Cancer Society (ACS), American College of Chest Physicians (ACCP), Canadian Task Force on Preventive Health Care (CTFPHC), and U.S. Preventive Services Task Force (USPSTF) recommendations for lung cancer screening in asymptomatic patients is provided in the tables below. The guidelines differ somewhat in scope and focus, with some of the guidelines offering recommendations beyond screening. For example, ACCP's lung cancer screening guideline represents just one chapter from a more comprehensive guideline supplement including recommendations related to lung cancer prevention, diagnosis, initial evaluation and staging, treatment, follow-up/surveillance, palliative treatment, and end of life care. In addition to the interventions compared in this synthesis (chest x-ray, sputum cytology, and low-dose computed tomography), the ACS, ACCP and USPSTF guidelines include discussion of other detection methods such as fluorescence bronchoscopy and biomolecular marker screening, though no formal recommendations regarding these techniques are made.

ACS released its guidance on early lung cancer detection in response to recommendations resulting from the 1998 International Conference on the Prevention and Early Diagnosis of Lung Cancer held in Varese, Italy which called for "national governments and public health organizations involved in cancer

prevention and control to more aggressively address tobacco control and to urgently consider the issues surrounding the early detection of lung cancer."

ACCP, CTFPHC, and USPSTF each considered ACS recommendations when developing and/or updating their own recommendations. ACCP also reviewed USPSTF's 2004 recommendations; CTFPHC likewise reviewed USPSTF's 1996 recommendations as well as the 2003 version of ACCP's guideline. USPSTF refers readers to recommendations issued by CTFPHC and ACS.

The tables below provide a side-by-side comparison of key attributes of each guideline, including specific interventions and practices that are addressed. The language used in these tables, particularly that which is used in Table 3, Table 4, and Table 5, is in most cases taken verbatim from the original guidelines.

- Table 1 provides a quick-view glance at the primary interventions considered by each group.
- Table 2 compares presents the overall scope of the guidelines., comparing the objectives, target populations, and intended users.
- Table 3 provides a more detailed comparison of the specific recommendations offered by each group for the topics under consideration in this synthesis
- Table 4 lists the potential benefits and harms associated with the implementation of each guideline as stated in the original guidelines.
- Table 5 presents the rating schemes used to rate the level of evidence and/or the strength of the recommendations. References supporting selected recommendations for the CTFPHC guidelines are also provided in this table.

A summary discussion of the areas of agreement and areas of differences among the guidelines is presented following the content comparison tables.

Listed below are common abbreviations used within the tables and discussions:

- ACCP, American College of Chest Physicians
- ACS, American Cancer Society
- CT, computed tomography
- CTFPHC, Canadian Task Force on Preventive Health Care
- CXR, Chest x-ray
- LDCT, low-dose computed tomography (i.e., spiral or helical computed tomography)
- USPSTF, United States Preventive Services Task Force

**TABLE 1: COMPARISON OF INTERVENTIONS AND PRACTICES CONSIDERED**
*("✓" indicates topic is addressed)*

| | ACS (2001) | ACCP (2007) | CTFPHC (2003) | USPSTF (2004) |
|---|---|---|---|---|
| CXR | ✓ | ✓ | ✓ | ✓ |

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| LDCT | ✓ | ✓ | ✓ | ✓ |
| Sputum cytology | ✓ | ✓ | | ✓ |

| TABLE 2: COMPARISON OF SCOPE AND CONTENT | |
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| **Objective and Scope** | |
| **ACS (2001)** | • To update health care professionals and the public on issues regarding testing for early lung cancer detection in light of emerging data on new imaging technologies |
| **ACCP (2007)** | • To provide updated, evidence-based, clinically relevant guidelines for the early detection of lung cancer |
| **CTFPHC (2003)** | • To update the 1994 recommendations of the Canadian Task Force of Preventive Health care for lung cancer screening<br>• To make recommendations on the effectiveness of chest radiographic examination and spiral computed tomography (CT) for lung cancer screening in asymptomatic patients |
| **USPSTF (2004)** | • To summarize the current U.S. Preventive Services Task Force (USPSTF) recommendation on screening for lung cancer and the supporting scientific evidence<br>• To update the 1996 recommendations contained in the *Guide to Clinical Preventive Services*, second edition |
| **Target Population** | |
| **ACS (2001)** | • United States<br>• Individuals at risk for the development of lung cancer, including current and/or former smokers |
| **ACCP (2003)** | • United States<br>• Individuals at risk for lung cancer but without symptoms or a history of cancer |
| **CTFPHC** | • Canada |

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| **(2003)** | • Asymptomatic adults with a history of smoking with no previous history of lung cancer |
| **USPSTF (2004)** | • United States<br>• Asymptomatic persons seen in primary care settings |
| **Intended Users** | |
| **ACS (2001)** | Advanced Practice Nurses; Allied Health Personnel; Health Care Providers; Health Plans; Hospitals; Managed Care Organizations; Nurses; Patients; Physician Assistants; Physicians; Public Health Departments |
| **ACCP (2007)** | Advanced Practice Nurses; Allied Health Personnel; Health Care Providers; Nurses; Patients; Physicians; Psychologists/Non-physician Behavioral Health Clinicians; Social Workers |
| **CTFPHC (2003)** | Advanced Practice Nurses; Allied Health Personnel; Physician Assistants; Physicians |
| **USPSTF (2004)** | Advanced Practice Nurses; Allied Health Personnel; Nurses; Physician Assistants; Physicians |

| **TABLE 3: COMPARISON OF RECOMMENDATIONS FOR LUNG CANCER SCREENING** | |
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| **ACS (2001)** | • The ACS **does not recommend** lung cancer screening for asymptomatic individuals at risk for lung cancer.<br>• However, individual physicians and patients may decide that the evidence is sufficient to warrant the use of screening tests on an individual basis.<br>• The ACS recommends that, to the extent possible, individuals at risk for lung cancer due to current or prior smoking history, history of significant exposure to second-hand smoke, or occupational history be aware of their continuing lung cancer risk. Those who seek testing for early lung cancer detection should be informed about what is currently known about the benefits, limitations, and risks associated with conventional and emerging early detection technologies, as well as the associated diagnostic procedures and treatment.<br>• Current technologies for detecting early lung cancer include imaging modalities (CXR, LDCT) and cytological and molecular evaluations of lung sputum.<br>• Results from screening studies using spiral CT have been regarded |

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| | as sufficiently encouraging to lead a growing number of institutions and facilities to promote CT screening to asymptomatic individuals at risk for lung cancer, with such promotion likely to increase. Since both media reports and local advertising may stimulate interest in spiral CT testing among health care providers and individuals at higher risk, the ACS has determined that updated guidance about early lung cancer detection is appropriate.<br>• Given the high rate of positive results that occur with CT screening for lung cancer and the complexity of the algorithm for working up small nodules, there is reason to be concerned about broad dissemination of lung screening outside of experienced, multi-specialty settings and prior to validation of this new technology. For this reason, it is critically important during this period of evolving investigations into the efficacy of spiral CT and other modalities that appropriate and influential professional organizations provide a foundation for best practices based upon the current state-of-the art, and also promote informed decision-making for patients about possible benefits, risks, and limitations of testing for early lung cancer detection. Individuals interested in early detection also should be encouraged to participate in trials. |
| **ACCP (2007)** | • We do not recommend that low-dose helical CT be used to screen for lung cancer except in the context of a well-designed clinical trial. Grade of recommendation, 2C<br>• We recommend against the use of serial CXR to screen for the presence of lung cancer. Grade of recommendation, 1A<br>• We recommend against the use of single or serial sputum cytologic evaluation to screen for the presence of lung cancer. Grade of recommendation, 1A |
| **CTFPHC (2003)** | *Chest X-ray*<br><br>The CTFPHC concludes that there is **fair** evidence to recommend against screening asymptomatic people for lung cancer using chest radiographic examination. **(D recommendation)** (Manser et al., 2002 [I, fair]; Kubik, Parkin, & Zatloukal, 2000 [I, fair]; Marcus et al., 2000 [I, fair]; Nishii et al., 2001 [II-2, fair]; Okamoto et al., 1999 [II-2, fair]; Sagawa et al., 2001 [II-2, fair]; Sobue, 2000 [II-2, fair]; Tsukada et al., 2001 [II-2, fair]).<br><br>*Low Dose Computed Tomography*<br><br>The CTFPHC concludes that there is **insufficient** evidence (in quantity and/or quality) to make a recommendation as to whether spiral CT scanning should be used for screening asymptomatic people for lung cancer. However, other factors may influence decision-making. **(I recommendation).** (Henschke et al., 1999; Henschke et al., 2001; Sone et al., 1998; Sone et al., 2001; Diederich et al., 2000 [II-2, III]). |

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| **USPSTF (2004)** | The USPSTF concludes that the evidence is insufficient to recommend for or against screening asymptomatic persons for lung cancer with either LDCT, CXR, sputum cytology, or a combination of these tests. **I recommendation**<br><br>**Clinical Considerations**<br><br>• The benefit of screening for lung cancer has not been established in any group, including asymptomatic high-risk populations such as older smokers. The balance of harms and benefits becomes increasingly unfavorable for persons at lower risk, such as nonsmokers.<br>• The sensitivity of LDCT for detecting lung cancer is 4 times greater than the sensitivity of CXR. However, LDCT is also associated with a greater number of false-positive results, more radiation exposure, and increased costs compared with CXR.<br>• Because of the high rate of false-positive results, many patients will undergo invasive diagnostic procedures as a result of lung cancer screening. Although the morbidity and mortality rates from these procedures in asymptomatic individuals are not available, mortality rates because of complications from surgical interventions in symptomatic patients reportedly range from 1.3 to 11.6%; morbidity rates range from 8.8 to 44%, with higher rates associated with larger resections.<br>• Other potential harms of screening are potential anxiety and concern as a result of false-positive tests, as well as possible false reassurance because of false-negative results. However, these harms have not been adequately studied. |

| **TABLE 4: BENEFITS AND HARMS OF LUNG CANCER SCREENING** | |
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| **Potential Benefits** | |
| **ACS (2001)** | Reduced mortality associated with lung cancer. |
| **ACCP (2007)** | Appropriate screening of patients at risk for lung cancer |
| **CTFPHC (2003)** | **Appropriate use of lung cancer screening in asymptomatic people may result in the following:**<br><br>• Decreased number of false-positives associated with screening tests<br>• Decreased risk of invasive diagnostic procedures to confirm suspicious or false-positive findings |

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| | • Prevention of exposure of the patient to unnecessary radiation<br>• Prevention of decreased motivation to stop smoking if a false-negative result is obtained<br><br>**Additional potential benefits of specific screening procedures**:<br><br>Spiral CT scanning provides the hope of a more sensitive screening test than CXR, and prospective studies have demonstrated an improved detection of smaller lesions. However, it is unclear whether improved detection will lead to improved mortality. |
| **USPSTF (2004)** | The USPSTF found fair evidence that screening with LDCT, CXR, or sputum cytology can detect lung cancer at an earlier stage than lung cancer would be detected in an unscreened population; however, the USPSTF found poor evidence that any screening strategy for lung cancer decreases mortality. |
| **Potential Harms** | |
| **ACS (2001)** | Not stated |
| **ACCP (2007)** | Not stated |
| **CTFPHC (2003)** | *Potential Harms of Not Screening*<br><br>May miss detection of early stage lung cancer<br><br>*Potential Harms of Screening*<br><br>In one reported study, 50% of positive CXRs were not suspicious for cancer on spiral CT and, from RCTs, even suspicious CXRs are often false positives after diagnostic workup (positive predictive values ranging from 41%-60%). Nevertheless, spiral CT picks up many more lesions, and 90-92% of "positive" CT scans turn out not to be cancerous. These patients are exposed not only to radiation, but also to the anxiety and risks involved in having a suspicious finding confirmed by invasive diagnostic procedures. The biopsy rate for spiral CT ranges from 11-12%, 24-26% of which prove to be non-cancerous. Another study reported that 18 CT scans were either falsely read as negative or did not pick up a cancer detected by sputum cytology, leading to a false negative rate of 45% of spiral CT.<br><br>False negatives carry with them a false reassurance and a risk that the patient will be less motivated to quit smoking. |
| **USPSTF (2004)** | • Because of the invasive nature of diagnostic testing and the possibility of a high number of false-positive tests in certain populations, there is potential for significant harms from |

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| | screening. Therefore, the USPSTF could not determine the balance between the benefits and harms of screening for lung cancer.<br>• Other potential harms of screening are potential anxiety and concern as a result of false-positive tests, as well as possible false reassurance because of false-negative results. However, these harms have not been adequately studied. |

| TABLE 5: EVIDENCE RATING SCHEMES AND REFERENCES | |
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| **ACCP (2007)** | **Quality of Evidence Scale**<br><br>**High (A)** Randomized controlled trials (RCTs) without important limitations or overwhelming evidence from observational studies<br><br>**Moderate (B)** RCTs with important limitations (inconsistent results, methodologic flaws, indirect, or imprecise) or exceptionally strong evidence from observational studies<br><br>**Low or very low (C)** Observational studies or case series<br><br>**Strength of Recommendations**<br><br>**1A** - Strong recommendation<br><br>**1B** - Strong recommendation<br><br>**1C** - Strong recommendation<br><br>**2A** - Weak recommendation<br><br>**2B** - Weak recommendation<br><br>**2C** - Weak recommendation |
| **CTFPHC (2003)** | **Levels of Evidence - Research Design Rating**<br><br>**I**: Evidence from randomized controlled trials (RCT)<br><br>**II-1**: Evidence from controlled trials without randomization<br><br>**II-2**: Evidence from cohort or case-control analytic studies, preferably from more than 1 centre or research group<br><br>**II-3**: Evidence from comparisons between times or places with or |

without the intervention; dramatic results in uncontrolled experiments could also be included here

**III**: Opinions of respected authorities, based on clinical experience, descriptive studies, or reports of expert committees

**Quality (Internal Validity) Rating**

**Good**: A study that meets all design-specific criteria* well

**Fair**: A study that does not meet (or it is not clear that it meets) at least one design-specific criterion* but has no known "fatal flaw"

**Poor**: A study that has at least one design-specific* "fatal flaw," or an accumulation of lesser flaws to the extent that the results of the study are not deemed able to inform recommendations

*General design-specific criteria are outlined in Harris RP, Helfand M, Woolf SH, Lohr KN, Mulrow CD, Teutsch SM, Atkins D. Current Methods of the U.S. Preventive Services Task Force: A Review of the Process. Am J Prev Med 2001;20(suppl 3):21-35.

**Recommendations Grades for Specific Clinical Preventive Actions**

**A**: The Canadian Task Force (CTF) concludes that there is good evidence to recommend the clinical preventive action.

**B**: The CTF concludes that there is fair evidence to recommend the clinical preventive action.

**C**: The CTF concludes that the existing evidence is conflicting and does not allow making a recommendation for or against use of the clinical preventive action; however, other factors may influence decision-making.

**D**: The CTF concludes that there is fair evidence to recommend against the clinical preventive action.

**E**: The CTF concludes that there is good evidence to recommend against the clinical preventive action.

**I**: The CTF concludes that there is insufficient evidence (in quantity and/or quality) to make a recommendation; however, other factors may influence decision-making.

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| | Cancer 2001 Nov 2;85(9):1326-31. PubMed |
| **USPSTF (2004)** | The USPSTF grades the quality of the overall evidence for a service on a 3-point scale (good, fair, poor):<br><br>**Good**<br><br>Evidence includes consistent results from well-designed, well-conducted studies in representative populations that directly assess effects on health outcomes.<br><br>**Fair**<br><br>Evidence is sufficient to determine effects on health outcomes, but the strength of the evidence is limited by the number, quality, or consistency of the individual studies, generalizability to routine practice, or indirect nature of the evidence on health outcomes.<br><br>**Poor**<br><br>Evidence is insufficient to assess the effects on health outcomes because of limited number or power of studies, important flaws in their design or conduct, gaps in the chain of evidence, or lack of information on important health outcomes.<br><br>The USPSTF grades its recommendations according to one of 5 classifications (A, B, C, D, I) reflecting the strength of evidence and magnitude of net benefit (benefits minus harms):<br><br>**A**<br><br>The USPSTF strongly recommends that clinicians provide [the service] to eligible patients. The USPSTF found good evidence that [the service] improves important health outcomes and concludes that benefits substantially outweigh harms.<br><br>**B**<br><br>The USPSTF recommends that clinicians provide [the service] to eligible patients. The USPSTF found at least fair evidence that [the service] improves important health outcomes and concludes that benefits outweigh harms.<br><br>**C**<br><br>The USPSTF makes no recommendation for or against routine provision of [the service]. The USPSTF found at least fair evidence that [the service] can improve health outcomes but concludes that the |

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| | balance of benefits and harms is too close to justify a general recommendation.<br><br>**D**<br><br>The USPSTF recommends against routinely providing [the service] to asymptomatic patients. The USPSTF found at least fair evidence that [the service] is ineffective or that harms outweigh benefits.<br><br>**I**<br><br>The USPSTF concludes that the evidence is insufficient to recommend for or against routinely providing [the service]. Evidence that [the service] is effective is lacking, of poor quality, or conflicting and the balance of benefits and harms cannot be determined. |

## GUIDELINE CONTENT COMPARISON

The American Cancer Society (ACS), American College of Chest Physicians (ACCP), Canadian Task Force on Preventive Health Care (CTFPHC) and the U.S. Preventive Services Task Force (USPSTF) present recommendations for screening for lung cancer based on evidence available at the time of each report and provide explicit reasoning behind their judgments. ACCP, CTFPHC, and USPSTF rate the quality of their recommendations and the type of evidence supporting them; CTFPHC also provides literature citations to support their major recommendations. ACS recommendations are provided in narrative form. Both ACCP and USPSTF include a review of the evidence supporting their recommendations. ACCP, CTFPHC, and USPSTF all provide comparisons with other national guidelines, including ACS's recommendations.

### Areas of Agreement

The four groups are in general agreement regarding the inappropriateness of routine lung cancer screening in asymptomatic individuals. ACS specifically recommends against any routine screening, while the other three make recommendations based on specific diagnostic tests. All guidelines note the need for more research into the effectiveness of screening for lung cancer, most notably, randomized controlled trials on LDCT. ACS and USPSTF mention the National Cancer Institute's Prostate, Lung, Colorectal, and Ovarian (PLCO) Cancer Screening Trial as a prospective study that may eventually provide additional insight. ACCP addresses the National Cancer Institute's National Lung Screening Trial (NLST).

*Chest X-ray*

None of the four guidelines recommends CXR to screen for lung cancer in asymptomatic patients. Both ACCP and CTFPHC explicitly recommend against screening for lung cancer with CXR, while USPSTF concludes that there is

insufficient evidence to recommend for or against screening for lung cancer with chest x-ray. Although ACS makes no specific recommendations concerning CXR, they do not recommend any routine screening, though they note that individual patients and physicians may decide that the evidence warrants screening on an individual basis.

*Low-Dose Computed Tomography*

All four guidelines agree directly or indirectly that LDCT is more sensitive than CXR in detecting lung cancer. Each group however, acknowledges that this greater test sensitivity may be associated with a higher rate of false positives, which may result in the use of additional diagnostic procedures that carry a significant risk of harms. Each of the guidelines further note that currently, the evidence is not yet sufficient to determine whether or not detection of smaller lung cancers with LDCT reduces lung cancer mortality.

ACCP does not recommend that LDCT be used to screen for lung cancer except in the context of a well-designed clinical trial. CTFPHC and USPSTF conclude that there is insufficient evidence to recommend for or against the use of LDCT to screen asymptomatic patients at risk for lung cancer. ACS expresses concern that this technology may disseminate broadly before the technology is validated and encourages individuals interested in early detection to participate in clinical trials.

*Sputum Cytology*

None of the four guidelines recommend the use of sputum cytology for screening for lung cancer. ACCP explicitly recommends against its use, while USPSTF finds insufficient evidence to recommend for or against the technology. ACS further notes that one disadvantage of this technology is that positive test results require additional testing to identify location of the cancer. CTFPHC offers no recommendations regarding sputum cytology.

*Smoking Cessation - Primary Prevention*

While not described in the table above, it is important to note that all of the developers included in this comparison emphasize that smoking cessation is the best way to reduce lung cancer mortality at this time.

**Areas of Differences**

While all four guidelines are in general agreement about the lack of evidence supporting the efficacy of lung cancer screening, ACS makes a distinction between its recommendation against mass screening and decisions made by individual patients and their doctors, noting that their recommendations are not intended to discourage individuals from having early detection tests if they and their doctors determine that testing is appropriate. However, ACS notes that because of increasing availability and promotion of testing, it is critically important that individuals who are interested in testing understand both the potential benefits of screening with LDCT, as well as potential harms associated with diagnostic procedures and treatment. ACS offers guidance for patients and their doctors, and discourages testing in a setting that is not linked to multidisciplinary specialty

groups for diagnosis and follow-up. ACS further states that individuals who decide to undergo testing should have access to state-of-the art testing and follow-up.

ACCP also notes that the election to screen an individual who is at risk for lung cancer should be based on shared, informed decision making between provider and patient.

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This Synthesis was prepared by ECRI on October 8, 2005. This synthesis was verified by: CTFPHC on November 2, 2005; ACCP on November 28, 2005; USPSTF on November 30, 2005; and ACS on December 2, 2005. This synthesis was revised on January 13, 2008 to update ACCP recommendations.

Internet citation: National Guideline Clearinghouse (NGC). Guideline synthesis: Screening for lung cancer. In: National Guideline Clearinghouse (NGC) [website]. Rockville (MD): 2005 Dec (revised 2008 Feb). [cited YYYY Mon DD]. Available: http://www.guideline.gov.

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Date Modified: 7/28/2008